REMARKS

Applicants have studied the Office Action of April 2, 2004 ("Office Action"). It is respectfully submitted that the application is in condition for allowance. Claims 42-54 and 56-65 are pending in the present application. Claims 42-54 and 56-61 were rejected in the Office Action; claims 62-64 have been indicated as withdrawn from consideration. Claims 42 and 56-60 have been amended by virtue of the present amendment. Claim 65 has been added. No new matter has been added. Allowance of the application in view of Applicants' amendment and the ensuing remarks is respectfully requested.

Claim 42 has been amended to correct informalities. As amended, claim 42 refers to "*pituitary tumor transforming gene (PTTG).*" Support for this amendment may be found throughout the specification; for example, at page 3, line 4 and at page 4, line 31.

Claim 56 has been amended to correct informalities. As amended, claim 56 refers to "*pituitary tumor transforming gene (PTTG).*" Support for this amendment may be found throughout the specification; for example, at page 3, line 4 and at page 4, line 31.

Claim 57 has been amended to correct informalities. As amended, claim 57 refers to "*pituitary tumor transforming gene (PTTG).*" Support for this amendment may be found throughout the specification; for example, at page 3, line 4 and at page 4, line 31.

Claim 58 has been amended to correct informalities. As amended, claim 58 refers to "*pituitary tumor transforming gene (PTTG).*" Support for this amendment may be found throughout the specification; for example, at page 3, line 4 and at page 4, line 31.

Claim 59 has been amended to correct informalities. As amended, claim 59 refers to "*pituitary tumor transforming gene (PTTG).*" Support for this amendment may be found throughout the specification; for example, at page 3, line 4 and at page 4, line 31.

Claim 60 has been amended to more particularly point out that which Applicants regard as their invention. As amended, claim 60 describes an "*animal model*" for studying "*the function and mode of action of pituitary tumor transforming gene (PTTG)*" in mammalian physiology. Support for this amendment may be found throughout the specification; for example, at page 24, lines 1-25 and in the Examples at page 25, line 1 through page 34, line 17. Claim 60 has been

further amended to correct informalities. As amended, claim 60 refers to "*pituitary tumor transforming gene (PTTG).*" Support for this amendment may be found throughout the specification; for example, at page 3, line 4 and at page 4, line 31.

New claim 65 has been added to more particularly describe one feature of Applicants' invention. Claim 65 describes an "*animal model*" for studying "*hyperglycemia, hypoinsulinaemia, hypoleptinemia, diabetes, chromosomal aneuploidy, premature centromere division, chromosomal damage, aberrant mitotic cellular division, thrombocytopenia, thymic hyperplasia, splenic hypoplasia, testicular hypoplasia, and female subfertility, or any combination thereof, at the cellular level, tissue level, organismal level or any combination thereof.*" Support for this amendment may be found throughout the specification; for example, at page 24, lines 1-25 and in the Examples at page 25, line 1 through page 34, line 17.

In the Office Action, Examiner objected to claims 42 and 56-60 because of informalities. Examiner indicated that the term "PTTG" needed to be spelled out. This objection is respectfully traversed.

As amended, each of Applicants' independent claims (i.e., claims 42 and 56-60) spells out the term "PTTG" as pituitary tumor transforming gene, and further includes a parenthetical listing the term "PTTG" as the abbreviation for pituitary tumor transforming gene. As such, Applicants respectfully submit that the amendments to claims 42 and 56-60 have remedied Examiner's objection, and therefore respectfully request withdrawal of this objection.

In the Office Action, Examiner rejected claim 60 under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. In particular, Examiner noted that the omitted steps are, "*how the null mutant mouse is going to be used in the study of mammalian physiology, [and] what kind of mammalian physiology phenomenon is being studied.*" This rejection is respectfully traversed.

As amended, Applicants' claim 60 now describes an "*animal model*" for studying "*the function and mode of action of pituitary tumor transforming gene (PTTG)*" in mammalian physiology, wherein the animal model incorporates the null mutant mouse of the present

invention. Applicants contemplate the use of such an animal model for examining the consequences resulting from the absence of PTTG protein. *See, e.g.*, Specification at page 24, lines 1-12. Applicants further describe various physiological phenomena and medical conditions that are the result of an absent or nonfunctional PTTG polypeptide in an organism; Applicants indicating that the PTTG null rodent of the present invention will be useful as a mammalian screening model for studying the mentioned and other physiological phenomena. *See, e.g.*, Id. Further support can be found, wherein Applicants describe the methods and effects of studying various physiological phenomena including diabetes, female fertility, thrombocytopenia and testicular, thymic, and splenic size in PTTG null mice. *See, e.g.*, Examples at page 25, line 1 through page 34, line 17. As such, Applicants respectfully submit that claim 60, as amended, along with each of the claims that depend therefrom comply with 35 U.S.C. § 112, second paragraph, and therefore respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 112, second paragraph.

In the Office Action, Examiner rejected claims 42-54 and 56-61 under 35 U.S.C. § 112, first paragraph, as lacking enablement. In particular, Examiner found that "*the specification does not disclose a repeatable process to obtain the claimed null mutant mice and it is not apparent if these are readily available to the public.*" This rejection is respectfully traversed.

Applicants respectfully submit that Examiner has underestimated the level of skill in the art in considering claims 42-54 and 56-61. A claim is enabled so long as an individual of reasonable skill in the art "*could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.*" United States v. Telectronics, Inc., 857 F.2d 778, 785 (Fed. Cir. 1988); MPEP § 2164.01. In fact, "*a patent need not teach, and preferably omits, what is well known in the art.*" (emphasis added). In re Buchner, 929 F.2d 660, 661 (Fed. Cir. 1991); MPEP § 2164.01. Moreover, "*the fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation.*" In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988).

Applicants respectfully submit that the claims, as presented, are enabled. Applicants' claims 42-54 and 56-61 describe a null mutant mouse with a null mutation on both PTTG alleles in the germ cells. Additionally, these null mutant mice each have at least one of the phenotypes

disclosed in the specification (*i.e.*, hyperglycemia, hypoinsulinaemia, hypoleptinemia, diabetes, chromosomal aneuploidy, premature centromere division, chromosomal damage, aberrant mitotic cellular division, thrombocytopenia, thymic hyperplasia, splenic hypoplasia, testicular hypoplasia or female subfertility).

Applicants respectfully submit that the level of skill in the relevant field of art (*i.e.*, genetic engineering) was tremendously high at the time of filing of the invention. Methods for creating a "null mutation" in germ cell or a "knockout" organism are known in the art, and commonly practiced by those working in the art at the time of the invention. *See, e.g.,* U.S. Patent No: 6,245,965 (describing methods of creating double null mammalian cells and knockout animals); U.S. Patent No: 6,218,595 (describing methods of creating DAT knockout mice); and U.S. Patent No: 5,981,830 (describing a method of creating a hepsin knockout mouse). Furthermore, guidance and teaching can be found in the literature; for example, in accordance with techniques known in the art, and particularly by means of in vivo homologous recombination, the literature teaches that it is feasible to systematically modify and/or express virtually any gene *in vivo* in a mouse. *See, e.g.*, Capecchi, M., "Altering the genome by homologous recombination," *Science*, Vol. 244, p. 1288-1292 (1989). By the nature of the specification and claims, one of skill in the art would recognize how to create the double null PTTG mouse of the present invention. As such, only routine experimentation would be required for one of skill in this highly specialized field of art to make and use Applicants' invention. Furthermore, the mice of the present invention can be readily screened for the presence of a double null mutation using the phenotypic characteristics disclosed in the specification. Applicants respectfully submit that based on the level of skill in the art along with the data disclosed in the specification and examples of the present application, the claims are enabled.

In the instant case, Applicants' specification includes detailed instructions and examples that would allow one of skill in the art to create the null mutant mice of the present invention. *See, e.g.,* page 25, line 1 through page 26, line 16. Examiner indicated that the specification does not disclose a repeatable process to obtain the claimed null mutant mice and that it is not apparent that the mice are readily available to the public. However, Applicants disclosure in the specification coupled with the knowledge in the art would allow one of skill in the art to create and test the null mutant mice of the present invention. Applicants respectfully remind Examiner that "*a patent need not teach, and preferably omits, what is well known in the art.*" (emphasis

added). In re Buchner, 929 F.2d 660, 661 (Fed. Cir. 1991); MPEP § 2164.01. Furthermore, any experimentation required in creating such a null mutant mouse is merely routine in this highly specialized field of art, even if it is substantial. This issue has been revisited on numerous occasions by the courts, and every time the answer is the same -- that even the need for substantial but routine experimentation does not preclude patentability on grounds of enablement.

In light of the foregoing remarks, Applicants respectfully submit that claims 42-54 and 56-61 are properly enabled, and therefore respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 112, first paragraph.

In the office action dated January 29, 2003, Examiner required election among five embodiments of Applicants' invention; identified as Groups I, II, III, IV and V. Applicants elected the claims of Group I for prosecution on the merits. In that office action, Examiner indicated that Applicants' original claim 1 linked the embodiments of their invention described in Group I to Groups III, IV and V, and further indicated that Applicants' original claims 27-31 linked the embodiments of their invention described in Groups III, IV and V to one another. Although each of these original linking claims has since been canceled, for purposes of restriction practice, Applicants' pending claims 56, 57, 58 and 60 are substantively similar to Applicants' original linking claims 28, 29, 30 and 31. Furthermore, Applicants' pending claims 62, 63 and 64 are substantively similar to Applicants' original claims 33, 34 and 35, which described the particular features of the restricted subject matter in Groups III, IV and V, respectively.

Applicants respectfully submit that claims 56-58 and 60 are each allowable, and therefore submit that the non-elected embodiments of their invention described in pending claims 62-64 must be rejoined and fully examined for patentability under 37 CFR 1.104 (MPEP § 809.04).

Applicants believe that the present amendment and foregoing remarks place the application in condition for allowance. A favorable action is respectfully requested. If for any reason Examiner finds the application other than in condition for allowance, Examiner is

requested to call the undersigned attorney at the Los Angeles telephone number (213) 488-7100 to discuss the steps necessary for placing the application in condition for allowance.

Respectfully submitted,
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Enclosure: Petition for One-Month Extension of Time